| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce Patent and Trademark Office                             | Atty. Docket No.      | Serial No. |
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| JUL 2 2 2004 W               | INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT  (Use several sheets if necessary) | 02-742-F<br>(400/132) | 10/665,951 |
| AND WORLD                    |   | Applicant:            |            |
|                              |   | McSwiggen et al.      |            |
|                              | ·   | Filing Date:          | Group:     |
|                              |   | September 18, 2003    | 1035       |

## **U.S. PATENT APPLICATION DOCUMENTS**

| Examiner<br>Initial |   | Document Number | Filing Date | Name                  | Class | Subclass | Publication<br>Date if<br>Appropriate  |
|---------------------|---|-----------------|-------------|-----------------------|-------|----------|--|
| Who                 | • | 09/226,044      | 07/12/01    | Hoffman et al.        |       |          |  |
| 1                   | • | 10/151,116      | 05/17/02    | Matulic-Adamic et al. |       |          | ···· · · · · · · · · · · · · · · · · · |
|                     | • | 10/201,394      | 08/13/01    | Vargeese et al.       |       |          |  |
|                     | * | 10/287,949      | 11/04/02    | Pavco                 |       |          |  |
|                     | * | 10/306,747      | 11/27/02    | Pavco                 |       |          |  |
|                     | • | 10/427,160      | 04/30/03    | Vargeese et al.       |       |          |  |
|                     | • | 10/438,493      | 05/15/03    | Pavco et al.          |       |          |  |
|                     | * | 10/444,853      | 05/23/03    | McSwiggen et al.      |       |          |  |
|                     | * | 10/664,668      | 09/16/03    | McSwiggen et al.      |       |          | 1                                      |
|                     | * | 10/664,767      | 09/16/03    | McSwiggen et al.      |       |          |  |
|                     | ٠ | 10/665,255      | 09/18/03    | McSwiggen et al.      |       |          |  |
|                     | • | 10/665,951      | 09/18/03    | McSwiggen et al.      |       |          |  |
|                     | • | 10/670,011      | 09/23/03    | McSwiggen et al.      |       |          |  |
|                     | • | 10/693,059      | 10/23/03    | McSwiggen et al.      |       |          |  |
|                     | ٠ | 10/712,633      | 11/13/03    | McSwiggen et al.      |       |          |  |
| V                   | • | 10/720,448      | 11/24/03    | McSwiggen et al.      |       |          |  |

| EXAMINER (HO) DATE CONSIDERED 10/11/05 |                          |
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|  | DATE CONSIDERED 10/11/05 |

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| FORM PTO-1449<br>(Rev. 2-32)                               | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.      | Serial No. |
|--|--|-----------------------|------------|
| INFORMATION DIS<br>STATEMENT BY A<br>(Use several sheets i | SCLOSURE<br>PPLICANT                                       | 02-742-F<br>(400/132) | 10/665,951 |
|  |  | Applicant:            |            |
| ·  |  | McSwiggen et al.      |            |
|  |  | Filing Date:          | Group:     |
| ·  |  | September 18, 2003    | 1635       |

| NHB | •  | 10/727,780   | 12/03/03 | Vaish et al.     |    | Ţ        |  |
|-----|----|--------------|----------|------------------|----|----------|--|
| 1   | •  | 10/757,803   | 01/14/04 | McSwiggen et al. |    |          |  |
|     | 1. | 10/758,155   | 01/12/04 | McSwiggen et al. |    |          |  |
|     | •  | 10/764,957   | 01/26/04 | McSwiggen et al. | -  |          |  |
|     | •  | 10/831,620   | 04/23/04 | McSwiggen et al. |    |          |  |
|     | 1. | 2001/0007666 | 07/12/01 | Hoffman et al.   |    |          |  |
|     | •  | 2002/0130430 | 09/19/02 | Castor           |    |          |  |
|     | •  | 2004/0037780 | 02/06/04 | Parsons et al.   |    |          |  |
|     | •  | 60/082,404   | 04/20/98 | Thomspon et al.  |    |          |  |
|     | •  | 60/334,461   | 11/30/01 | Pavco            |    |          |  |
| :   | •  | 60/358,580   | 02/20/02 | Beigelman et al. | _  |          |  |
|     | •  | 60/363,124   | 03/11/02 | Beigelman et al. |    |          |  |
|     | 1. | 60/386,782   | 06/06/02 | Beigelman et al. |    |          |  |
|     | •  | 60/393,796   | 07/03/02 | McSwiggen et al. | ε. | <u> </u> |  |
|     | •  | 60/399,348   | 07/29/02 | McSwiggen et al. |    |          |  |
|     | •  | 60/402,996   | 08/13/02 | Usman et al.     |    |          |  |
|     | •  | 60/406,784   | 08/29/02 | Beigelman et al. |    |          |  |
| :   | •  | 60/408,378   | 09/05/02 | Beigelman et al. |    |          |  |
|     | •  | 60/409,293   | 09/09/02 | Beigelman et al. |    |          |  |

| EXAMINER Office | DATE CONSIDERED 1011 | 105 |
|-----------------|----------------------|-----|

| FORM PTO-1449 (Rev. 2-32)  U.S. Department of Commerce Patent and Trademark Office  INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (Use several sheets if necessary) |   |            |          | Atty. Docket No. Serial No. 10/665,951 (400/132) |                                 |          |
|--|---|------------|----------|--|---------------------------------|----------|
|  |   |            |          |  | Applicant:  McSwiggen et al.    |          |
|  |   |            |          |  | Filing Date: September 18, 2003 | Group:   |
| ruhr   | * | 60/440,129 | 01/15/03 | Beigelman et al.                                 |                                 |          |
| Otho   | * | 60/543,480 | 02/10/04 | Jadhav et al.                                    |                                 | <u> </u> |

## **U.S. PATENT DOCUMENTS**

| Examiner<br>Initial |   | Document<br>Number | Date     | Name             | Class | Subclass | Filing<br>Date if<br>Appropriate |
|---------------------|---|--------------------|----------|------------------|-------|----------|----------------------------------|
| Oxto                | * | 4,501,729          | 02/26/85 | Boucher et al.   |       |          |                                  |
|                     | • | 5,138,045          | 08/11/92 | Cook et al.      |       |          |                                  |
|                     | * | 5,214,136          | 05/25/93 | Lin et al.       |       |          |                                  |
|                     | * | 5,334,711          | 08/02/94 | Sproat et al.    |       |          |                                  |
|                     | * | 5,624,803          | 04/29/97 | Noonberg et al.  |       |          |                                  |
| v                   | • | 5,627,053          | 05/06/97 | Usman et al.     |       |          |                                  |
|                     | * | 5,631,360          | 05/20/97 | Usman et al.     |       |          |                                  |
|                     | * | 5,670,633          | 09/23/97 | Cook et al.      |       |          |                                  |
|                     | * | 5,672,695          | 09/30/97 | Eckstein et al.  | -     |          |                                  |
|                     | • | 5,716,824          | 02/10/98 | Beigelman et al. |       |          |                                  |
|                     | * | 5,792,847          | 08/11/98 | Buhr et al.      |       |          |                                  |
|                     | * | 5,804,683          | 09/08/98 | Usman et al.     |       |          |                                  |
|                     | • | 5,814,620          | 09/29/98 | Robinson et al.  |       |          |                                  |

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| FORM PTO-1449<br>(Rev. 2-32)          | U.S. Department of Commerce Patent and Trademark Office | Atty. Docket No.   | Serial No. |
|---------------------------------------|---|--------------------|------------|
|                                       |   | 02-742-F           | 10/665,951 |
| INFORMATION DISCI<br>STATEMENT BY APP |   | (400/132)          | -          |
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|                                       |   | Applicant:         |            |
|                                       | •   | McSwiggen et al.   |            |
| ·                                     |   | Filing Date:       | Group:     |
|                                       |   | September 18, 2003 | 1635       |

| OHB | • | 5,831,071 | 11/03/98 | Usman et al.          |  |  |
|-----|---|-----------|----------|-----------------------|--|--|
|     | • | 5,854,038 | 12/29/98 | Sullenger et al.      |  |  |
|     | • | 5,889,136 | 03/30/99 | Scaringe et al.       |  |  |
| ; , | • | 5,898,031 | 04/27/99 | Crooke                |  |  |
|     | • | 5,902,880 | 05/11/99 | Thompson              |  |  |
|     | • | 5,998,203 | 12/07/99 | Adamic et al.         |  |  |
|     | • | 6,001,311 | 12/14/99 | Brennen               |  |  |
|     | • | 6,005,087 | 12/21/99 | Cook et al.           |  |  |
|     | • | 6,008,400 | 12/28/99 | Scaringe et al.       |  |  |
|     | • | 6,054,576 | 04/25/00 | Bellon et al.         |  |  |
|     | • | 6,107,094 | 08/22/00 | Crooke                |  |  |
|     | ٠ | 6,111,086 | 08/29/00 | Scaringe et al.       |  |  |
|     | • | 6,117,657 | 09/12/00 | Usman et al.          |  |  |
|     | • | 6,146,886 | 11/14/00 | Thompson et al.       |  |  |
|     | • | 6,153,737 | 11/28/00 | Manoharan et al.      |  |  |
|     | • | 6,162,909 | 12/19/00 | Bellon et al.         |  |  |
|     | • | 6,180,613 | 01/30/01 | Kaplitt et al.        |  |  |
|     |   | 6,235,310 | 05/22/01 | Wang et al.           |  |  |
| V   | • | 6,248,878 | 06/19/01 | Matulic-Adamic et al. |  |  |

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|-------------------------|-------------------|

| FORM PTO-<br>(Rev. 2-32) | 1449 | INFORMA<br>STATEM |          | ANT                  | Atty. Docked 02-742-F (400/132)  Applicant: McSwiggen Filing Date September | et al.   | Sheet 5 of 29  Serial No.  10/665,951  Group: |
|--------------------------|------|-------------------|----------|----------------------|---|----------|---|
| OHR                      | ٠    | 6,300,074         | 10/09/01 | Gold et al.          |   | T        |   |
| M                        | *    | 6,303,773         | 10/16/01 | Bellon et al.        |   |          |   |
|                          | •    | 6,335,434         | 01/01/02 | Guzaev et al.        |   |          |   |
|                          | •    | 6,353,098         | 03/05/02 | Usman et al.         |   |          |   |
|                          | ٠    | 6,362,323         | 03/26/01 | Usman et al.         |   |          |   |
|                          | •    | 6,395,713         | 05/28/02 | Beigelman et al.     |   |          |   |
|                          | *    | 6,437,117         | 08/20/02 | Usman et al.         |   | 1        |   |
|                          | •    | 6,447,796         | 09/10/02 | Vook et al.          |   |          |   |
|                          | ٠    | 6,469,158         | 10/22/02 | Usman et al.         |   |          |   |
|                          | •    | 6,476,205         | 11/05/02 | Buhr et al.          |   |          |   |
|                          | ٠    | 6,506,559         | 01/14/03 | Fire et al.          |   |          |   |
|                          | *    | 6,528,631         | 03/04/03 | Cook et al.          |   |          |   |
|                          | ٠    | 6,565,885         | 05/20/03 | Tarara et al.        |   |          |   |
|                          | *    | 6,582,728         | 06/24/03 | Platz et al.         |   |          |   |
|                          | *    | 6,586,524         | 07/01/03 | Sagara               |   |          |   |
|                          | •    | 6,592,904         | 07/15/03 | Platz et al.         |   |          |   |
|                          |      |                   | FORE     | IGN PATENT DOCUMENTS |   |          |   |
|                          |      | Document          | Date     | Country              | Class   | Subclass | Translation                                   |
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| FORM PTO-1449<br>(Rev. 2-32) |   | ent of Commerce<br>Trademark Office | Atty. Docket No.   | Serial No.   |
|------------------------------|---|-------------------------------------|--------------------|--------------|
|                              |   |                                     | 02-742-F           | 10/665,951   |
| ll ,                         | NFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT |                                     | (400/132)          |              |
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|                              |   |                                     | Applicant:         | <del>.</del> |
|                              |   | •                                   | McSwiggen et al.   |              |
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|------|-----|-----------|----------|-----------------------|-----|-----|----|
|      |     |           |          |                       |     | Yes | No |
| OHYS | 1.  | 4037501   | 08/03/00 | AU (Kreutzer et al.)  |     |     |    |
|      | 2.  | 2,359,180 | 08/03/00 | CA (Kreutzer et al.)  |     |     |    |
|      | 3.  | 1144623   | 08/03/00 | EP (Kreutzer et al.)  |     |     |    |
|      | 4.  | 89/02439  | 03/23/89 | WO (Arnold et al.)    |     |     |    |
|      | 5.  | 90/14090  | 11/29/90 | WO (Gillespie et al.) |     |     |    |
|      | 6.  | 91/03162  | 03/21/91 | WO (Rossi et al.)     |     |     |    |
|      | 7.  | 92/07065  | 04/30/92 | WO (Eckstein et al.)  |     |     |    |
|      | 8.  | 93/15187  | 08/05/93 | WO (Usman et al.)     |     |     |    |
|      | 9.  | 93/23569  | 11/25/93 | WO (Draper et al.)    |     |     |    |
|      | 10. | 94/02595  | 02/03/94 | WO (Sullivan et al.)  |     |     |    |
|      | 11. | 94/01550  | 01/20/94 | WO (Agrawal et al.)   |     |     | •  |
|      | 12. | 95/06731  | 03/09/95 | WO (Usman et al.)     |     |     |    |
|      | 13. | 95/11910  | 05/04/95 | WO (Dudycz et al.)    |     |     |    |
|      | 14. | 96/10390  | 04/11/96 | WO (Ansell et al.)    |     |     |    |
|      | 15. | 96/10391  | 04/11/96 | WO (Choi et al.)      |     |     |    |
|      | 16. | 96/10392  | 04/11/96 | WO (Holland et al.)   |     |     |    |
|      | 17. | 96/18736  | 06/20/96 | WO (Beigelman et al.) | 1 . |     |    |
| V    | 18. | 97/26270  | 07/24/97 | WO (Wincott et al.)   |     |     |    |

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| FORM PTO-144<br>(Rev. 2-32) | 9                                    |                       | 6. Department of Commerce atent and Trademark Office | Atty. Docket No.   | Serial No. |
|-----------------------------|--------------------------------------|-----------------------|--|--------------------|------------|
| ·                           | INFORMAT<br>STATEMEI<br>(Use several | 02-742-F<br>(400/132) | 10/665,951   |                    |            |
|                             | ,                                    | Applicant:            |  |                    |            |
|                             |                                      |                       |  | McSwiggen et al.   |            |
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| Mara I                      | T                                    | <del></del>           |  |                    |            |
| (KB) 19.                    | 98/13526                             | 04/02/98              | WO (Woolf et al.)                                    |                    |            |

| OHB | 19. | 98/13526 | 04/02/98 | WO (Woolf et al.)                    | · <del></del> |   |     |
|-----|-----|----------|----------|--------------------------------------|---------------|---|-----|
|     | 20. | 99/07409 | 02/18/99 | WO (Deschamps de<br>Pailette et al.) |               |   |     |
|     | 21. | 99/14226 | 03/25/99 | WO (Wengel et al.)                   |               |   |     |
|     | 22. | 99/31262 | 06/24/99 | WO (Barry et al.)                    |               |   |     |
|     | 23. | 99/32619 | 07/01/99 | WO (Fire et al.)                     |               |   | • . |
|     | 24. | 99/49029 | 09/30/99 | WO (Graham et al.)                   |               |   |     |
|     | 25. | 99/53050 | 10/21/99 | WO (Waterhouse et al.)               |               |   |     |
|     | 26. | 99/54459 | 10/28/99 | WO (Thompson et al.)                 |               |   |     |
|     | 27. | 99/61631 | 12/02/99 | WO (Heifetz et al.)                  |               |   |     |
|     | 28. | 00/01846 | 01/13/00 | WO (Plaetinck et al.)                | -             |   |     |
|     | 29. | 00/44895 | 08/03/00 | WO (Kreutzer et al.)                 |               |   | -   |
|     | 30. | 00/44914 | 08/03/00 | WO (Li et al. )                      |               |   |     |
|     | 31. | 00/49035 | 08/24/00 | WO (Sheen)                           |               |   |     |
|     | 32. | 00/53722 | 09/14/00 | WO (O'Hare et al.)                   |               |   |     |
|     | 33. | 00/63364 | 10/26/00 | WO (Pachuk et al.)                   |               |   |     |
|     | 34. | 00/66604 | 11/09/00 | WO (Wengel et al.)                   | <br>          | 1 |     |
|     | 35. | 01/04313 | 01/18/01 | WO (Satishchandran et al.)           |               |   |     |
|     | 36. | 01/29058 | 04/26/01 | WO (Mello et al.)                    |               |   | -   |
| V   | 37. | 01/36646 | 05/25/01 | WO (Zernicka-Goetz et al.)           |               |   |     |

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| 111 | FORM PTO-1449<br>(Rev. 2-32) |     |                       |                              | S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.   | Serial No.<br>10/665,951 |
|-----|------------------------------|-----|-----------------------|------------------------------|--|--------------------|--------------------------|
|     |                              |     | INFORMATI<br>STATEMEN | (400/132)                    |  |                    |                          |
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|     |                              |     | ·                     | Applicant:  McSwiggen et al. |  |                    |                          |
|     |                              |     |                       |                              |  | Filing Date:       | Group:                   |
| L.  |                              |     |                       |                              |  | September 18, 2003 | 3   1035                 |
| At  | B                            | 38. | 01/38551              | 05/31/01                     | WO (Grossniklaus et al.)                                 |                    |                          |
|     | 1                            | 39. | 01/42443              | 06/14/01                     | WO (Churikov et al.)                                     |                    |                          |
|     |                              | 40. | 01/49844              | 07/12/01                     | WO (Driscoll et al.)                                     |                    |                          |
|     |                              | 41. | 01/53475              | 07/26/01                     | WO (Cogoni et al.)                                       |                    |                          |
|     |                              | 42. | 01/68836              | 09/20/01                     | WO (Beach et al.)  |                    |                          |
|     |                              | 43. | 01/70944              | 09/27/01                     | WO (Honer et al.)  |                    |                          |
|     |                              | 44. | 01/70949              | 09/27/01                     | WO (Graham et al.)                                       |                    |                          |
| :   |                              | 45. | 01/72774              | 10/04/01                     | WO (Deak et al.)   |                    |                          |
|     |                              | 46. | 01/75164              | 10/11/01                     | WO (Tuschl et al.)                                       |                    |                          |
|     |                              | 47. | 01/92513              | 12/06/01                     | WO (Arndt et al.)  |                    |                          |
|     |                              | 48. | 01/96584              | 12/20/01                     | WO (Mushegian et al.)                                    |                    |                          |
|     |                              | 49. | 02/055692             | 07/18/02                     | WO (Kreutzer et al.)                                     |                    |                          |
|     |                              | 50. | 02/055693             | 07/18/02                     | WO (Kreutzer et al.)                                     |                    |                          |
|     |                              | 51. | 02/22636              | 03/21/02                     | WO (Bennett et al.)                                      |                    |                          |
|     |                              | 52. | 02/38805              | 05/15/02                     | WO (Echeverri et al.)                                    |                    |                          |
|     | L                            | 53. | 02/44321              | 06/06/02                     | WO (Tuschl et al.)                                       |                    |                          |

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WO (Pavco)

WO (Alheim et al.)

WO (Wang et al.)

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Sheet 9 of 29

|  |                  |             |                                       |                                   |   |   | Sheet 9 of 2             |
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| FORM PTO-1449 (Rev. 2-32) INFORMATION DISCLOSTATEMENT BY APPLI |                  |             |                                       |                                   |   | Atty. Docket No.<br>02-742-F<br>(400/132) | Serial No.<br>10/665,951 |
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|  |                  |             |                                       | Applicant:                        |   |   |                          |
| ı  |                  |             |                                       | McSwiggen et al.                  |   |   |                          |
|  |                  |             |                                       | Filing Date:                      | Group:  |   |                          |
|  |                  |             |                                       | <del></del>                       |   | September 18, 2003                        | 1635                     |
| OH1  | 2 5              | 57.         | 03/47518                              | 06/12/03                          | WO (Wang et al.)                              |   | <u> </u>                 |
| Uii :  | _                | 58.         | PCT/US02/15876                        | 05/20/02                          | Beigelman et al.                              | -   |                          |
|  | <del>-   `</del> | 59.         | PCT/US02/17674                        | 05/29/02                          | WO (Pavco et al.)                             | <del> </del>                              |                          |
|  |                  | 50.         | PCT/US03/05022                        | 02/20/03                          | WO (McSwiggen et al.)                         | †   | <del></del>              |
|  | $\epsilon$       | 51.         | PCT/US03/05028                        | 02/20/03                          | McSwiggen et al.                              |   |                          |
|  | 6                | 62.         | PCT/US03/05346                        | 02/20/03                          | McSwiggen et al.                              |   |                          |
| 1  | 6                | 53.         | WO 03/064625                          | 02/03/03                          | WO (Woolf et al.)                             |   |                          |
| $\exists$  | E                | 64.         | WO 03/064626                          | 02/03/03                          | WO (Woolf et al.)                             |   | 1                        |
| $\exists$  | 6                | <b>35</b> . | WO 03/030989                          | 04/17/03                          | WO (Behar et al.)                             |   |                          |
|  | E                | 66.         | WO 03/043689                          | 05/03/03                          | WO (Behar et al.)                             |   |                          |
| J  | / E              | <b>57</b> . | WO 04/013280                          | 05/26/03                          | WO (Davidson et al.)                          |   |                          |
|  |                  |             | OTHER DOCU                            | MENTS (Inci                       | uding Author, Title, Date, Per                | tinent Pages, Etc).                       |                          |
| JAK  | b 6              | 58. ·       | Adah et al., "Che<br>Medicinal Chemis | mistry and Bio<br>stry, 8, 1189-1 | chemistry of 2',5'-Oligoadenyla<br>212 (2001) | ate-Based Antisense St                    | rategy," Current         |
| 1  | 6                | <b>59</b> . | Aiello et al., "Vas                   | cular Endothe                     | lial Growth Factor in Ocular Flu              | uid of Patients with Diab                 | etic Retinopathy         |

## 69. Aiello et al., "Vascular Endothelial Growth Factor in Ocular Fluid of Patients with Diabetic Retinopathy and Other Retinal Disorders," The New England Journal of Medicine 331(22):1480-1487 (1994) 70. Akhtar and Juliano, "Cellular Uptake and Intracellular Fate of AntiSense Oligonucleotides," Trends Cell Biol. 2:139-144 (1992 71. Aldrian-Herrada et al., "A peptide nucleic acid (PNA) is more rapidly internalized in cultured neurons

when coupled to a retro-inverso delivery peptide. The antisense activity depresses the target mRNA and

| EXAMINER DATE CONSIDERED 11 00 |                      |
|--------------------------------|----------------------|
| 10(11)                         | DATE CONSIDERED 1105 |

protein in magnocellular oxytocin neurons," Nucleic Acids Research 26:4910-4916 (1998)

Sheet 10 of 29

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.      | Serial No. |  |
|------------------------------|--|-----------------------|------------|--|
|                              |  | 02-742-F<br>(400/132) | 10/665,951 |  |
|                              | INFORMATION DISCLOSURE STATEMENT BY APPLICANT              | (400) 102)            |            |  |
|                              | (Use several sheets if necessary)                          |                       |            |  |
|                              | •  | Applicant:            |            |  |
|                              |  | McSwiggen et al.      |            |  |
|                              | •  | Filing Date:          | Group:     |  |
|                              |  | September 18, 2003    | 1635       |  |

| 0 | HB. | 72.              | Allshire, "RNAi and Heterochromatin - A Hushed-up Affair," Science 297:1818-1819 (2002)  |
|---|-----|------------------|--|
|   |     | <sup>-</sup> 73. | Andrews and Faller, "A rapid micropreparation technique for extraction of DNA-binding proteins from limiting numbers of mammalian cells," Nucleic Acids Research 19:2499 (1991)                                  |
|   |     | 74.              | Autiero et al., "Role of PIGF in the intra- and intermolecular cross talk between the VEGF receptors Flt1 and Flk1," Nature Medicine, 9:936-943 (2003)   |
|   |     | 75.              | Baenziger and Fiete, "Galactose and N-Acetylgalactosamine-Specific Endocytosis of Glycopeptides by Isolated Rat Hepatocytes," Cell 22:611-620 (1980)   |
|   |     | 76.              | Bahramian et al., "Transcriptional and Posttranscriptional Silencing of Rodent $\sigma$ 1(I) Collagen by a Homologous Transcriptionally Self-Silenced Transgene," Molecular and Cellular Biology, 274-283 (1999) |
|   |     | 77.              | Bannai et al., "Effect of Injection of Antisense of Oligodeoxynucleotides of GAD Isozymes into Rat Ventromedial Hypothalamus on Food Intake and Locomotor Activity," <u>Brain Research</u> 784:305-315 (1998)    |
|   |     | 78.              | Bannai et al., "Water-absorbent Polymer as a Carrier for a Discrete Deposit of Antisense Oligodeoxynucleotides in the Central Nervous System," <u>Brain Research Protocols</u> 3:83-87 (1998)                    |
| Ц |     | 79.              | Bass, "The short answer," Nature 411:428-429 (2001)  |
|   |     | 80.              | Bass, "Double-Stranded RNA as a Template for Gene Silencing," Cell, 101, 235-238 (2000)  |
|   |     | 81.              | Beaucage and Iyer, "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives," Tetrahedron 49:1925-1963 (1993)  |
|   |     | 82.              | Beigelman et al., "Chemical Modification of Hammerhead Ribozymes," The Journal of Biological Chemistry 270:25702-25708 (1995)  |
|   |     | 83.              | Bellon et al., "Amino-Linked Ribozymes: Post-Synthetic Conjugation of Half-Ribozymes," Nucleosides & Nucleotides 16:951-954 (1997)   |
| \ | 1   | 84.              | Bellon et al., "Post-synthetically Ligated Ribozymes: An Alternative Approach to Iterative Solid Phase Synthesis," Bioconjugate Chem. 8:204-212 (1997)   |

| EXAMINER QTM | DATE CONSIDERED | 10/11/05 |
|--------------|-----------------|----------|

Sheet 11 of 29

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce Patent and Trademark Office                          | Atty. Docket No.                | Serial No. |
|------------------------------|--|---------------------------------|------------|
|                              | INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (Use several sheets if necessary) | 02-742-F<br>(400/132)           | 10/665,951 |
|                              | (Coo constantinosos in incocosary)   | Applicant:  McSwiggen et al.    |            |
|                              |  | Filing Date: September 18, 2003 | Group:     |

| alts | 85. | Berkman et al., "Expression of the Vascular Permeability Factor/Vascular Endothelial Growth Factor Gene in Central Nervous System Neoplasms," The Journal of Clinical Investigation, Inc. 91:153-159 (1993)        |  |
|------|-----|--|--|
| ;    | 86. | Bernstein et al., "Role for a Bidentate Ribonuclease in the Initiation Step of RNA Interference," Nature 409:363-366 (2001)  |  |
|      | 87. | Bettinger et al., "Size Reduction of Galactosylated PEI/DNA Complexes Improves Lectin-Mediated Gene Transfer into Hepatocytes," <i>Bioconjugate Chem.</i> , 10, 558-561 (1999)                                     |  |
|      | 88. | Boado et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," Journal of Pharmaceutical Sciences 87:1308-1315 (1998)                                   |  |
|      | 89. | Boado, "Antisense drug delivery through the blood-brain barrier," Advanced Drug Delivery Reviews 15:73-107 (1995)  |  |
|      | 90. | Brennan et al., "Two-Dimensional Parallel Array Technology as a New Approach to Automated Combinatorial Solid-Phase Organic Synthesis," Biotechnology and Bioengineering (Combinatorial Chemistry) 61:33-45 (1998) |  |
|      | 91. | Broaddus et al., "Distribution and stability of antisense phosphorothioate oligonucleotides in rodent brain following direct intraparenchymal controlled-rate infusion," <u>J Neurosurg</u> 88:734-742 (1998)      |  |
|      | 92. | Brody and Gold, "Aptamers as therapeutic and diagnostic agents," Reviews in Molecular Biotechnology 74:5-13 (2000)   |  |
|      | 93. | Burger et al., "Experimental Corneal Neovascularization: Biomicroscopic, Angiographic, and Morphologic Correlation," Cornea 4:35-41 (1985/1986)  |  |
|      | 94. | Burgin et al., "Chemically Modified Hammerhead Ribozymes with Improved Catalytic Rates," Biochemistry 35:14090-14097 (1996) (volume no. mistakenly listed as 6)  |  |
|      | 95. | Burlina et al., "Chemical Engineering of RNase Resistant and Catalytically Active Hammerhead Ribozymes," Bioorganic & Medicinal Chemistry 5:1999-2010 (1997)   |  |
| Y    | 96. | Caruthers et al., "Chemical Synthesis of Deoxyoligonucleotides and Deoxyoligonucleotide Analogs," Methods in Enzymology 211:3-19 (1992)  |  |

| EXAMINER | (1)(1-0 | DATE CONSIDERED      |
|----------|---------|----------------------|
|          | 114160  | DATE CONSIDERED 1011 |
|          | (XIII)  | lound                |

Sheet 12 of 29

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce Patent and Trademark Office | Atty. Docket No.   | Serial No. |
|------------------------------|---|--------------------|------------|
|                              |   | 02-742-F           | 10/665,951 |
| INFORMATIO                   | ON DISCLOSURE   | (400/132)          |            |
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|                              |   | McSwiggen et al.   |            |
|                              |   | Filing Date:       | Group:     |
|                              |   | September 18, 2003 | 1635       |

| arb  | 97.  | Chen et al., "Multitarget-Ribozyme Directed to Cleave at up to Nine Highly Conserved HIV-1 env RNA Regions Inhibits HIV-1 Replication-Potential Effectiveness Against Most Presently Sequenced HIV-1 Isolates," Nucleic Acids Research 20:4581-4589 (1992) |
|------|------|--|
|      | 98.  | Chiu et al., "siRNA function in RNAi: A chemical modification analysis," RNA, 9:1034-1048 (2003)   |
|      | 99.  | Choi et al., "Effect of Poly(ethylene glycol) Grafting on Polyethylenimine as a Gene Transfer Vector in vitro," Bull. Korean Chem. Soc., 22, 46-52 (2001)  |
| 100. |      | Chowrira et al., "In Vitro and in Vivo Comparison of Hammerhead, Hairpin, and Hepatitis Delta Virus Self-Processing Ribozyme Cassettes," J. Biol. Chem. 269:25856-25864 (1994)   |
|      | 101. | Clark and Yoria, "Ophthalmic Drug Discovery," Nature, 2, 448-459 (2003)  |
|      | 102. | Clemens et al., "The Double-Stranded RNA-Dependent Protein Kinase PKR:Structure and Function," J. Interferon & Cytokine Res., 17, 503-524 (1997)   |
|      | 103. | Cload and Schepartz, "Polyether Tethered Oligonucleotide Probes," J. Am. Chem. Soc. 113:6324-6326 (1991)   |
|      | 104. | Connolly et al., "Binding and Endocytosis of Cluster Glycosides by Rabbit Hepatocytes," The Journ. of Biol. Chem. 257:939-945 (1982)   |
|      | 105. | Conry et al., "Phase I Trial of a Recombinant Vaccinia Virus Encoding Carcinoembryonic Antigen in Metastatic Adenocarcinoma: Comparison of Intradermal versus Subcutaneous Administration," Clinical Cancer Research 5:2330-2337 (1999)                    |
|      | 106. | Couture and Stinchcomb, "Anti-gene therapy: the use of ribozymes to inhibit gene function," Trends In Genetics 12:510-515 (1996)   |
|      | 107. | Detmar et al., "Overexpression of Vascular Permeability Factor/Vascular Endothelial Growth Factor and its Receptors in Psoriasis," J. Exp. Med. 180:1141-1146 (1994)   |
| y    | 108. | Diebold et al., "Mannose Polyethylenimine Conjugates for Targeted DNA Delivery into Dendritic Cells*," The Journal of Biological Chemistry, 274, 19087-19094 (1999)  |

|          | f     |                 |      |
|----------|-------|-----------------|------|
| EXAMINER | ather | DATE CONSIDERED | Mula |

Sheet 13 of 29

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce Patent and Trademark Office                          | Atty. Docket No.      | Serial No. |
|------------------------------|--|-----------------------|------------|
|                              | INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (Use several sheets if necessary) | 02-742-F<br>(400/132) | 10/665,951 |
|                              | ,  | Applicant:            |            |
|                              |  | McSwiggen et al.      |            |
|                              |  | Filing Date:          | Group:     |
|                              |  | September 18, 2003    | 1651       |

| OHB | 109. | Dropulic et al., "Functional Characterization of a U5 Ribozyme: Intracellular Suppression of Human Immunodeficiency Virus Type I Expression," Journal of Virology 66:1432-1441 (1992)  |
|-----|------|--|
|     | 110. | Durand et al., "Circular Dichroism Studies of an Oligodeoxyribonucleotide Containing a Hairpin Loop Made of a Hexaethylene Glycol Chain: Conformation and Stability," Nucleic Acids Research 18:6353-6359 (1990) [sometimes referred to as Seela and Kaiser] |
|     | 111. | Earnshaw et al., "Modified Oligoribonucleotides as Site-Specific Probes of RNA Structure and Function," Biopolymers 48:39-55 (1998)  |
|     | 112. | Economides et al., Cytokine traps: multi-componetnt, high-affinity blockers of cytokine action," <i>Nature Medicine</i> , 9, 1, 47-52 (2003)   |
|     | 113. | Elbashir et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," Nature 411:494-498 (2001)  |
| ,   | 114. | Elbashir et al., "Functional Anatomy of siRNAs for Mediating Efficient RNAi in Drosophila Melanogaster Embryo Lysate," The EMBO Journal 20:6877-6888 (2001)  |
|     | 115. | Elbashir et al., "RNA Interference is Mediated by 21- and 22-Nucleotide RNAs," Genes and Development 15:188-200 (2001)   |
|     | 116. | Elkins and Rossi, "Ch. 2 - Cellular Delivery of Ribozymes," in Delivery Strategies for Antisense Oligonucleotide Therapeutics, edited by Akhtar, CRC Press, pp. 17-220 (1995)  |
|     | 117. | Elroy-Stein and Moss, "Cytoplasmic Expression System Based on Constitutive Synthesis of Bacteriophage T7 RNA Polymerase in Mammalian Cells," Proc. Natl. Acad. Sci. USA 87:6743-6747 (1990)  |
|     | 118. | Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide) Microshperes Implanted Into the Brain," Cell Transplantation 8:47-58 (1999)  |
|     | 119. | Epa et al., "Downregulation of the p75 Neurotrophin Receptor in Tissue Culture and <i>In Vivo</i> , Using β-Cyclodextrin-Adamantane-Oligonucleotide Conjugates," <i>Anitsense Nuc. Acid Drug Dev.</i> , 10:469-478 (2000)                                    |

|       | DATE CONSIDERED | 10)11/10 |
|-------|-----------------|----------|
| MIDIO |                 | 1011119  |

Sheet 14 of 29

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.   | Serial No. |
|------------------------------|--|--------------------|------------|
|                              |  | 02-742-F           | 10/665,951 |
|                              | INFORMATION DISCLOSURE STATEMENT BY APPLICANT              | (400/132)          |            |
|                              | (Use several sheets if necessary)                          |                    |            |
|                              |  | Applicant:         |            |
|                              |  | McSwiggen et al.   |            |
|                              |  | Filing Date:       | Group:     |
| <u>.</u>                     |  | September 18, 2003 | 1035       |

| OHB      | 120. | Erbacher et al., "Transfection and physical properties of various sacccharide, poly(ethylene glycol), and antibody-derivatized polyethylenimines (PEI), <i>The Journal of Gene Medicine</i> , 1, 210-222 (1999) [sometimes incorrectly cited as pages 1-18] |
|----------|------|---|
|          | 121. | Fava et al., "Vascular Permeability Factor/Endothelial Growth Factor (VPF/VEGF): Accumulation and Expression in Human Synovial Fluids and Rheumatoid Synovial Tissue," J. Exp. Med. 180:341-346 (1994)  |
|          | 122. | Ferentz and Verdine, "Disulfied Cross-Linked Oligonucleotides," J. Am. Chem. Soc. 113:4000-4002 (1991)  |
|          | 123. | Filleur et al., "SiRNA-mediated Inhibition of Vascular Endothelial Growth Factor Severely Limits Tumor Resistance to Antiangiogenic Thrombospondin-1 and Slows Tumor Vascularization and Growth," Cancer Research, 63, 3919-3922 (2003)                     |
|          | 124. | Fire et al., "Potent and Specific Genetic Interference by Double-Stranded RNA in Caenorhabditis Elegans," Nature 391:806-811(1998)  |
|          | 125. | Fire, "RNA-triggered Gene Silencing," TIG 15:358-363(1999)  |
|          | 126. | Folkman et al., "Long-term Culture of Capillary Endothelial Cells," Proc. Natl. Acad. Sci. USA 76:5217-5221 (1979)  |
|          | 127. | Folkman, Judah, "Tumor Angiogenesis," Advances in Cancer Research 43:175-203 (1985)   |
|          | 128. | Freier et al., "Improved free-energy parameters for predictions of RNA duplex stability," Proc. Natl. Acad. Sci. USA 83:9373-9377 (1986) [sometimes referred to as Frier]   |
|          | 129. | Furgeson et al., "Modified Linear Polyethylenimine—Cholesterol Conjugates for DNA Complexation,"<br>Bioconjugate Chem., 14, 840-847 (2003)  |
|          | 130. | Futami et al., "Induction fo apoptosis in HeLa cells with siRNA expression vector targeted against bcl-2," Nucleic Acids Research Supplement, 251-252 (2002)  |
|          | 131. | Gao and Huang, "Cytoplasmic Expression of a Reporter Gene by Co-Delivery of T7 RNA Polymerase and T7 Promoter Sequence with Cationic Liposomes," Nucleic Acids Research 21:2867-2872 (1993)   |
| <b>Y</b> | 132. | Genbank Accession No. AF020393  |

| EXAMINER | Otto | DATE CONSIDERED | Miles |
|----------|------|-----------------|-------|
|          |      |                 |       |

Sheet 15 of 29

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce Patent and Trademark Office                          | Atty. Docket No.      | Serial No. |
|------------------------------|--|-----------------------|------------|
|                              | INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (Use several sheets if necessary) | 02-742-F<br>(400/132) | 10/665,951 |
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|                              |  | McSwiggen et al.      |            |
| ·                            |  | Filing Date:          | Group:     |
|                              |  | September 18, 2003    | 1085       |

| ONTO | 133. | Genbank Accession No. AF022375 |
|------|------|--------------------------------|
|      | 134. | Genbank Accession No. AF024710 |
|      | 135. | Genbank Accession No. AF035121 |
|      | 136. | Genbank Accession No. AF063657 |
|      | 137. | Genbank Accession No. AF063658 |
|      | 138. | Genbank Accession No. AF092125 |
|      | 139. | Genbank Accession No. AF092126 |
|      | 140. | Genbank Accession No. AF092127 |
|      | 141. | Genbank Accession No. AF095785 |
|      | 142. | Genbank Accession No. AF098331 |
|      | 143. | Genbank Accession No. AF437895 |
|      | 144. | Genbank Accession No. AF468110 |
|      | 145. | Genbank Accession No. AF486837 |
|      | 146. | Genbank Accession No. AH006909 |
|      | 147. | Genbank Accession No. AJ000185 |
|      | 148. | Genbank Accession No. AJ010438 |
|      | 149. | Genbank Accession No. AY047581 |
|      | 150. | Genbank Accession No. D89630   |
| Y    | 151. | Genbank Accession No. E13256   |

|          | <del></del> |                 |      |
|----------|-------------|-----------------|------|
| EXAMINER | attor       | DATE CONSIDERED | Bulg |

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce Patent and Trademark Office                          | Atty. Docket No.                   | Serial No. |
|------------------------------|--|------------------------------------|------------|
| ·                            | INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (Use several sheets if necessary) | 02-742-F<br>(400/132)              | 10/665,951 |
|                              |  | Applicant:  McSwiggen et al.       |            |
| :                            |  | Filing Date:<br>September 18, 2003 | Group:     |

| <u> </u> |      |   |
|----------|------|---|
| DHB      | 152. | Genbank Accession No. E13332  |
|          | 153. | Genbank Accession No. E14000  |
|          | 154. | Genbank Accession No. E14233  |
|          | 155. | Genbank Accession No. E15156  |
|          | 156. | Genbank Accession No. E15157  |
|          | 157. | Genbank Accession No. NM_002019   |
|          | 158. | Genbank Accession No. NM_002020   |
|          | 159. | Genbank Accession No. NM_002253   |
|          | 160. | Genbank Accession No. NM_003376   |
|          | 161. | Genbank Accession No. NM_003377   |
|          | 162. | Genbank Accession No. NM_004469   |
|          | 163. | Genbank Accession No. NM_005429   |
|          | 164. | Genbank Accession No. U01134  |
|          | 165. | Genbank Accession No. X62568  |
|          | 166. | Genbank Accession No. X94216  |
|          | 167. | Genbank Accession No. Y08736  |
|          | 168. | Godbey et al., "Poly(ethylenimine) and its role in gene delivery," Journal of Controlled Release, 60, 149-160 (1999)  |
|          | 169. | Godbey et al., "Tracking the intracellular path of poly(ethylenimine)/DNA complexes for gene delivery,"<br><i>Proc. Natl. Acad. Sci. USA</i> , 96, 5177-5181 (1999) |
| <b>Y</b> | 170. | Gold et al., "Diversity of Oligonucleotide Functions," Annu. Rev. Biochem. 64:763-797 (1995)  |
|          |      |   |

| EXAMPLE | DATE CONSIDERED DILLO |
|---------|-----------------------|
|         |                       |

Sheet 17 of 29

| U.S. Department of Commerce Patent and Trademark Office  INFORMATION DISCLOSURE STATEMENT BY APPLICANT  Use several sheets if necessary) | Atty. Docket No.<br>02-742-F<br>(400/132)  | Serial No.<br>10/665,951 |
|--|--|--------------------------|
| ,,-,   | Applicant:  McSwiggen et al.  Filing Date: | Group:                   |
|  | September 18, 2003                         | 165                      |

| ars      | 171. | Gonzalez et al., "New Class of Polymers for the Delivery of Macromolecular Therapeutics," Bioconjugate Chem. 10:1068-1074 (1999)   |
|----------|------|--|
|          | 172. | Good et al., "Expression of small, therapuetic RNAs in human nuclei," Gene Therapy 4:45-54 (1997)  |
|          | 173. | Grant et al., "Insulin-like growth factor I acts as an angiogenic agent in rabbit cornea and retina: comparative studies with basic fibroblast growth factor," Diabetologia 36:282-291 (1993)                              |
| ·        | 174. | Hall et al., "Establishment and Maintenance of a Heterochromatin Domain," Science 297:2232-2237 (2002)   |
|          | 175. | Hamilton, et al., "A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants," Science, 286, 950-952 (1999)   |
|          | 176. | Hammond et al., "An RNA-Directed Nuclease Mediates Post-Transcriptional Gene Silencing in Drosophila Cells," Nature 404:293-296 (2000)   |
|          | 177. | Harborth et al., "Sequence, Chemical, and Structural Variation of Small Interfering RNAs and Short Hairpin RNAs and the Effect on Mammalian Gene Silencing," Antisense and Nucleic Acid Drug Development, 13:83-105 (2003) |
|          | 178. | Hermann and Patel, "Adaptive Recognition by Nucleic Acid Aptamers," Science 287:820-825 (2000)   |
|          | 179. | Hofland and Huang, "Formulation and Delivery of Nucleic Acids," Handbook of Exp. Pharmacol. 137:165-192 (1999)   |
|          | 180. | Hunziker et al., "Nucleic Acid Analogues: Synthesis and Properties, in Modern Synthetic Methods," VCH, 331-417 (1995)  |
|          | 181. | Hutvagner and Zamore, "A MicroRNA in a Multiple-Turnover RNAi Enzyme Complex," Science 297:2056-2060 (2002)  |
|          | 182. | Hutvagner et al., "A Cellular Function for the RNA-Interference Enzyme Dicer in the Maturation of the let-7 Small Temporal RNA," Science 293:834-838 (2001)  |
| <b>y</b> | 183. | International Search Report for PCT/US03/05028 mailed October 17, 2003   |

| EXAMINER ON THE STATE OF THE ST | DATE CONSIDERED | Mulos |
|--|-----------------|-------|

Sheet 18 of 29

| FORM PTO-1449<br>(Rev. 2-32) |  | nt of Commerce<br>rademark Office | Atty. Docket No.      | Serial No. |
|------------------------------|--|-----------------------------------|-----------------------|------------|
|                              |  |                                   | 02-742-F<br>(400/132) | 10/665,951 |
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|                              |  |                                   | Filing Date:          | Group:     |
|                              |  |                                   | September 18, 2003    | 1635       |

| M   | B           | 184. | International Search Report for PCT/US03/05346 mailed October 17, 2003   |
|-----|-------------|------|--|
|     |             | 185. | Ishiwata et al., "Physical-Chemistry Characteristics and Biodistribution of Poly(ethylene glycol)-Coated Liposomes Using Poly(oxyethylene) Cholesteryl Ether," Chem. Pharm. Bull. 43:1005-1011 (1995) (mistakenly referred to as Ishiwataet) |
|     |             | 186. | Izant and Weintraub, "Constitutive and Conditional Suppression of Exogenous and Endogeneous Genes by Anti-Sense RNA," Science 229:345-352 (1985)   |
|     |             | 187. | Jaschke et al., "Automated Incorporation of Polyethylene Glycol into Synthetic Oligonucleotides," Tetrahedron Letters 34:301-304 (1993) (sometimes mistakenly referred to as Jschke)   |
|     | -           | 188. | Jayasena, "Aptamers: An Emerging Class of Molecules that Rival Antibodies in Diagnostics," Clinical Chemistry 45:1628-1650 (1999)  |
| 189 |             | 189. | Jenuwein, "An RNA-Guided Pathway for the Epigenome," Science 297:2215-2218 (2002)  |
|     |             | 190. | Jolliet-Riant and Tillement, "Drug transfer across the blood-brain barrier and improvement of brain delivery," Fundam. Clin. Pharmacol. 13:16-26 (1999)  |
|     |             | 191. | Karle et al., "Differential Changes in Induced Seizures After Hippocampal Treatment of Rats with an Antisense Oligodeoxynucleotide to the GABA Receptor y2 Subunit," <u>Euro. Jour. of Pharmacology</u> 340:153-160 (1997)                   |
|     |             | 192. | Karpeisky et al, "Highly Efficient Synthesis of 2'-O-Amino Nucleosides And Their Incorporation in Hammerhead Ribozymes," Tetrahedron Letters 39:1131-1134 (1998)   |
|     |             | 193. | Kashani-Sabet et al., "Reversal of the Malignant Phenotype by an Anti-ras Ribozyme," Antisense Research & Development 2:3-15 (1992)  |
|     |             | 194. | Kaspareit-Rittinghausen et al., "Animal Model of Human Disease: Hereditary Polycystic Kidney Disease," Amer. Journ. of Pathology 139:693-696 (1991)  |
|     | <b>&gt;</b> | 195. | Kim et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumour growth in vivo," Nature 362:841-844 (1993)  |

\*

| EXAMINER ON THE STATE OF THE ST | DATE CONSIDERED | Mula |
|--|-----------------|------|
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Sheet 19 of 29

| FORM PTO-1449<br>(Rev. 2-32)             | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.      | Serial No. |
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| INFORMATION STATEMENT B (Use several she | DISCLOSURE<br>Y APPLICANT                                  | 02-742-F<br>(400/132) | 10/665,951 |
|  | ,,   | Applicant:            |            |
|  |  | McSwiggen et al.      | •          |
|  | •  | Filing Date:          | Group:     |
|  |  | September 18, 2003    | 1635       |

| OMB      | 196. | Koch et al., "Vascular Endothelial Growth Factor," Journal of Immunology 152:4149-4156 (1994)  |
|----------|------|--|
| 197.     |      | Kusser, "Chemically modified nucleic acid aptamers for in vitro selections: evolving evolution," Reviews in Molecular Biotechnology 74:27-38 (2000)  |
|          | 198. | Kwak et al., "VEGF Is Major Stimulator in Model of Choroidal Neovascularization," Investigative Ophthalmology & Visual Science, 41(10), 3158-3164 (2000)   |
| :        | 199. | Lasic and Needham "The 'Stealth' Liposome: A Prototypical Biomaterial," Chemical Reviews 95:2601-2627 (1995)   |
|          | 200. | Lasic and Papahadjopoulos, "Liposomes Revisited," Science 267:1275-1276 (1995)   |
|          | 201. | Lee and Larson, "Modified Liposome Formulations for Cytosolic Delivery of Macromolecules," ACS Symposium Series 752:184-192 (2000)   |
|          | 202. | Lee and Lee, "Preparation of Cluster Glycosides of N-Acetylgalactosamine That Have Subnanomolar Binding Constants Towards the Mammalian Hepatic Gal/GalNAc-specific Receptor," Glyconjugates J. 4:317-328 (1987) |
|          | 203. | Lee et al., "Expression of Small Interfering RNA's Targeted Against HIV-1 rev Transcripts in Human Cells," Nature Biotechnology 19:500-505 (2002)  |
|          | 204. | Leirdal et al., "Gene silencing in mammalian cells by preformed small RNA duplexes," Biochemical and Biophysical Research Communications, 295, 744-748 (2002)  |
|          | 205. | Lepri et al., "Effect of Low Molecular Weight Heparan Sulphate on Angiogenesis in the Rat Cornea after Chemical Cauterization," Journal of Ocular Pharmacology 10:273-281 (1994)                                 |
|          | 206. | L'Huillier et al., "Cytoplasmic Delivery of Ribozymes Leads to Efficient Reduction in $\alpha$ -Lactalbumin mRNA Levels in C1271 Mouse," EMBO J. 11:4411-4418 (1992)   |
| <b>Y</b> | 207. | Lieber et al., "Stable High-Level Gene Expression in Mammalian Cells by T7 Phage RNA Polymerase," Methods Enzymol. 217:47-66 (1993)  |

| EXAMINER | althor | DATE CONSIDERED | Milly |
|----------|--------|-----------------|-------|
|          |        |                 |       |

Sheet 20 of 29

| FORM PTO-1449<br>(Rev. 2-32)          | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.   | Serial No. |
|---------------------------------------|--|--------------------|------------|
|                                       |  | 02-742-F           | 10/665,951 |
| INFORMATION DISCL<br>STATEMENT BY APP |  | (400/132)          |            |
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|                                       |  | Applicant:         |            |
|                                       |  | McSwiggen et al.   |            |
|                                       |  | Filing Date:       | Group:     |
|                                       |  | September 18, 2003 | 1635       |

| OMP | 208. | Limbach et al., "Summary: the modified nucleosides of RNA," Nucleic Acids Research 22(12):2183-2196 (1994)  |
|-----|------|---|
|     | 209. | Lin and Matteucci, "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acid," J. Am. Chem. Soc. 120:8531-8532 (1998)   |
|     | 210. | Lin et al., "A Novel mRNA-cRNA Interference Phenomenon for Silencing bcl-2 Expression in Human LNCaP Cells," Biochemical and Biophysical Research Communications, 281, 639-644 (2001)   |
|     | 211. | Lin et al., "Policing Rogue Genes", Nature 402:128-129 (1999)   |
|     | 212. | Lisziewicz et al., "Inhibition of Human Immunodeficiency Virus Type 1 Replication by Regulated Expression of a Polymeric Tat Activation Response RNA Decoy as a Strategy for Gene Therapy in AIDS," Proc. Natl. Acad. Sci. U.S.A. 90:8000-8004 (1993) |
|     | 213. | Liu et al., "Cationic Liposome-mediated Intravenous Gene Delivery," J. Biol. Chem. 270(42):24864-24870 (1995)   |
|     | 214. | Loakes, "The Applications of Universal DNA Base Analogues," Nucleic Acids Research 29:2437-2447 (2001)  |
|     | 215. | Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach. 2. Generation of Covalently Closed, Double-Stranded Cyclic HIV-1 TAR RNA Analogs with High Tat-Binding Affinity," Nucleic Acids Research 21:2585-2589 (1993)    |
|     | 216. | Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach," Biochemistry 32:1751-1758 (1993)   |
|     | 217. | Martinez et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi," Cell 110:563-574 (2002)  |
|     | 218. | Maurer et al., "Lipid-based systems for the intracellular delivery of genetic drugs," Molecular Membrane Biology 16:129-140 (1999)  |
| 4   | 219. | McCurdy et al., "Deoxyoligonucleotides with Inverted Polarity: Synthesis and Use in Triple-Helix Formation" Nucleosides & Nucleotides 10:287-290 (1991)   |

| EXAMINER | affor | DATE CONSIDERED | Dula |
|----------|-------|-----------------|------|

Sheet 21 of 29

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce Patent and Trademark Office | Atty. Docket No.   | Serial No. |
|------------------------------|---|--------------------|------------|
| •                            |   | 02-742-F           | 10/665,951 |
| 4                            | ION DISCLOSURE<br>IT BY APPLICANT                       | (400/132)          |            |
| (Use several                 | sheets if necessary)                                    |                    |            |
|                              |   | Applicant:         | ·          |
|                              |   | McSwiggen et al.   |            |
|                              |   | Filing Date:       | Group:     |
|                              |   | September 18, 2003 | 1635       |

| 220. | McGarry and Lindquist, "Inhibition of heat shock protein synthesis by heat-inducible antisense RNA," Proc. Natl. Acad. Sci. USA 83:399-403 (1986)   |
|------|---|
| 221. | McLaren et al., "Vascular Endothelial Growth Factor (VEGF) Concentrations are Elevated in Peritoneal Fluid of Women with Endometriosis," Human Reproduction 11:220-223 (1996)   |
| 222. | McLaren et al., "Vascular Endothelial Growth Factor is Produced by Peritoneal Fluid Macrophages in Endometriosis and Is Regulated by Ovarian Steroids," J. Clin. Invest. 98:482-489 (1996)                            |
| 223. | McManus et al., "Gene Silencing Using Micro-RNA Designed Hairpins," RNA 8:842-850 (2002)  |
| 224. | Mesmaeker et al, "Novel Backbone Replacements for Oligonucleotides," American Chemical Society, pp. 24-39 (1994)  |
| 225. | Millauer et al., "Glioblastoma growth inhibited in vivo by a dominant-negative Flk-1 mutant," Letters to Nature 367:576-579 (1994)  |
| 226. | Miller et al., "Vascular Endothelial Growth Factor/Vascular Permeability Factor is Temporally and Spatially Correlated with Ocular Angiogenesis in a Primate Model," American Journal of Pathology 145:574-584 (1994) |
| 227. | Miyagishi and Taira, "U6 Promoter-driven siRNAs with Four Uridine 3' Overhangs Efficiently Suppress Targeted Gene Expression in Mammalian Cells," Nature Biotechnology 19:497-500 (2002)                              |
| 228. | Moore and Sharp, "Site-Specific Modification of Pre-mRNA: The 2'-Hydroxyl Groups at the Splice Sites," Science 256:992-996 (1992)   |
| 229. | Mori et al., "Inhibition of Chorodial Neovascularization by Intravenous Injection of Adenoviral Vectors Expressing Secretable Endostatin," American Journal of Pathology, 159(1), 313-320 (2001)                      |
| 230. | Mori et al., "Pigment epithelium-derived factor inhibits retinal and choroidal neovacularization," Journal of Cellular Physiology, 118(2) 253-263 (2001)  |
| 231. | Noonberg et al., In vivo generation of highly abundant sequence-specific oligonucleotides for antisense and triplex gene regulation," Nucleic Acids Research 22(14):2830-2836 (1994)                                  |
|      | 221. 222. 223. 224. 225. 226. 227. 228. 229.  |

| EXAMINER DATE CONSIDERED DILLE |          |       |                 |       |
|--------------------------------|----------|-------|-----------------|-------|
|                                | EXAMINER | athan | DATE CONSIDERED | Milly |

**Sheet 22 of 29** 

| FORM PTO-1449<br>(Rev. 2-32)                                  | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.      | Serial No. |
|---|--|-----------------------|------------|
| INFORMATION DISC<br>STATEMENT BY AP<br>(Use several sheets if | CLOSURE<br>PPLICANT  | 02-742-F<br>(400/132) | 10/665,951 |
| (333 3313/41 31103/31   | or corolar shoots if moscossary,                           | Applicant:            |            |
|   |  | McSwiggen et al.      |            |
|   |  | Filing Date:          | Group:     |
|   |  | September 18, 2003    | 1685       |

| THIS | 232. | Norrby, "Angiogenesis: new aspects relating to its initiation and control," APMIA 105:417-437 (1997)  |
|------|------|---|
|      | 233. | Novina et al., "siRNA-Directed Inhibition of HIV-1 Infection," Nature Medicine 1-6 (2002)   |
|      | 234. | Nykanen et al., "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," Cell 107:309-321 (2001)   |
|      | 235. | Ohkawa et al., "Activities of HIV-RNA Targeted Ribozymes Transcribed From a 'Shot-Gun' Type Ribozyme-trimming Plasmid," Nucleic Acids Symp. Ser. 27:15-16 (1992)  |
|      | 236. | Ohno-Matsui, et al., "Inducible Expression of Vascular Endothelial Growth Factor in Adult Mice Causes Severe Proliferative Retinopathy and Retinal Detachment," <i>Animal Models</i> from the Departments of Ophthalmology and Neuroscience and Molecular Biology and Genetics, <i>Am. J. Pathology</i> , 160, 711-719 (2002) |
|      | 237. | Ojwang et al., "Inhibition of Human Immunodeficiency Virus Type 1 Expression by a Hairpin Ribozyme," Proc. Natl. Acad. Sci. USA 89:10802-10806 (1992)   |
|      | 238. | Oku et al., "Real-time analysis of liposomal trafficking in tumor-bearing mice by use of positron emission tomography," Biochimica et Biophysica Acta 1238:86-90 (1995)   |
|      | 239. | Ono et al., "DNA Triplex Formation of Oligonucleotide Analogues Consisting of Linker Groups and Octamer Segments That Have Opposite Sugar-Phosphate Backbone Polarities," Biochemistry 30:9914-9921 (1991)  |
|      | 240. | O'Reilly et al., "Angiostatin: A Novel Angiogenesis Inhibitor That Mediates the Suppression of Metastases by a Lewis Lung Carcinoma," Cell 79:315-328 (1994)  |
|      | 241. | Orgis et al., "DNA/polyethylenimine transfection particles: Influence of ligands, polymer size, and PEGylation on internalization and gene expression," <i>AAPS PharmSci.</i> , 3 (3) article 21 (http://www.pharmsci.org) p. 1- 11 (2001)  |
|      | 242. | Ormerod et al., "Effects of Altering the Eicosanoid Precursor Pool on Neovascularization and Inflammation in the Alkali-burned Rabbit Cornea," American Journal of Pathology 137:1243-1252 (1990)   |
|      | 243. | Pal-Bhadra et al., "Heterochromatic Silencing and HP1 Localization in <i>Drosophila</i> Are Dependent on the RNAi Machinery," <i>Science</i> , 303, 669-672 (2004)  |

| EXAMINER () | DATE CONSIDERED ON THE |
|-------------|------------------------|

Sheet 23 of 29

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Comm<br>Patent and Trademark O | office                | Serial No. |
|------------------------------|---|-----------------------|------------|
|                              | NFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT   | 02-742-F<br>(400/132) | 10/665,951 |
|                              | (Use several sheets if necessary)                 | Applicant:            |            |
|                              |   | McSwiggen et al.      |            |
|                              |   | Filing Date:          | Group:     |
|                              |   | September 18, 2003    | 1635       |

| ans        | 244. | Pandey et al., "Role ov B61, the Ligand for the Eck Receptor Tyrosine Kinase, in TNF-α-Induced Angiogenesis," Science 268:567-569 (1995)  |
|------------|------|---|
|            | 245. | Pardridge et al., "Vector-mediated delivery of a polyamide ("peptide") nucleic acid analogue through the blood-brain barrier in vivo," Proc. Natl. Acad. Sci. USA 92:5592-5596 (1995)   |
|            | 246. | Parrish, "Functional Anatomy of a dsRNA Trigger: Differential Requirement for the Two Trigger Strands in RNA Interference," Molecular Cell 6:1077-1087 (2000)   |
|            | 247. | Passaniti et al., "A Simple, Quantitative Method for Assessing Angiogenesis and Antiangiogenic Agents Using Reconstituted Basement Membrane, Heparin, and Fibroblast Growth Factor," Laboratory Investigation 67:519-528 (1992)         |
|            | 248. | Paul et al., "Effective Expression of Small Interfering RNA in Human Cells," Nature Biotechnology 20:505-508 (2002)   |
|            | 249. | Perreault et al., "Mixed Deoxyribo- and Ribo-Oligonucleotides with Catalytic Activity," Nature 344:565-567 (1990) (often mistakenly listed as Perrault)   |
|            | 250. | Petersen et al., "Polyethylenimine-graft-Poly(ethylene glycol) Copolymers: Influence of Copolymer Block Structure on DNA Complexation and Biological Activities as Gene Delivery System, <i>Bioconjugate Chem.</i> , 13, 845-854 (2002) |
|            | 251. | Pieken et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," Science 253:314-317 (1991)  |
| ·          | 252. | Pierce et al., "Vascular endothelial growth factor/vascular permeability factor expression in a mouse model of retinal neovascularization," Proc. Natl. Acad. Sci. USA 92:905-909 (1995)  |
|            | 253. | Plate, "Vascular endothelial growth factor is potential tumor angiogenesis factor in human gilomas in vivo," Nature 359:845-848 (1992)  |
|            | 254. | Ponpipom et al., "Cell-Specific Ligands for Selective Drug Delivery to Tissues and Organs," J. Med. Chem. 24:1388-1395 (1981)   |
| \ <u>\</u> | 255. | Rajakumar et al., "Effects of Intrastriatal Infusion of D <sub>2</sub> Receptor Antisense Oligonucleotide on Apomorphine-Induced Behaviors in the Rat," <u>Synapse</u> 26:199-208 (1997)  |
|            |      |   |

| EXAMINER | OHM? | DATE CONSIDERED 11 |  |
|----------|------|--------------------|--|
|          |      |                    |  |

Sheet 24 of 29

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.      | Serial No. |
|------------------------------|--|-----------------------|------------|
|                              | 1  | 02-742-F<br>(400/132) | 10/665,951 |
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|                              |  | Applicant:            |            |
|                              |  | McSwiggen et al.      |            |
|                              |  | Filing Date:          | Group:     |
|                              |  | September 18, 2003    | 1035       |

| CUTP | 256. | Reich et al., "Small Interfering RNA (siRNA) targeting VEGF effectively inhibits ocular neovascularization in a mouse model," <i>Molecular Vision</i> , 9, 210-216 (2003)   |
|------|------|---|
|      | 257. | Reinhart and Bartel, "Small RNAs Correspond to Centromer Heterochromatic Repeats," Science 297:1831 (2002)  |
|      | 258. | Reinhart et al., "MicroRNAs in Plants," Genes & Development 16:1616-1626 (2002)   |
|      | 259. | Reynolds et al., "Rational siRNA designe for RNA intereference," <i>Nature Biotechnology</i> , 22, 3, 326-330 (2004)  |
|      | 260. | Richardson and Schepartz, "Tethered Oligonucleotide Probes. A Strategy for the Recognition of Structured RNA," J. Am. Chem. Soc. 113:5109-5111 (1991)   |
|      | 261. | Saenger (ed), "Modified Nucleosides and Nucleotides; Nucleoside Di- and Triphosphates; Coenzymes and Antibiotics, (ch.7)" Principles of Nucleic Acid Structure 158-200 (1984)   |
|      | 262. | Sarver et al., "Ribozymes as Potential Anti-HIV-1 Therapeutic Agents" Science 247:1222-1225 (1990)  |
|      | 263. | Scanlon et al., "Ribozyme-Mediated Cleavage of c-fos mRNA Reduces Gene Expression of DNA Synthesis Enzymes and Metallothionein," Proc. Natl. Acad. Sci. USA 88:10591-10595 (1991)   |
|      | 264. | Scaringe et al., "Chemical synthesis of biologically active oligoribonucleotides using β-cyanoethyl protected ribonucleoside phosphoramidites," Nucl Acids Res. 18:5433-5441 (1990)   |
| ٠    | 265. | Schroeder et al., "Diffusion Enhancement of Drugs by Loaded Nanoparticles in Vitro," Prog. Neuro-Psychopharmacol. & Biol. Psychiat. 23:941-949 (1999) [sometimes cited by RPI as Prog Neuropsychopharmacol Biol Psychiatry 23:941-949, 1999 |
|      | 266. | Schwarz et al., "Evidence that siRNAs Function as Guides, Not Primers, in the Drosophila and Human RNAi Pathways," Molecular Cell 10:537-548 (2002)   |
|      | 267. | Schwarz et al., "Asymmetry in the Assembly of the RNAi Enzyme Complex," Cell, 1115, 199-208 (2003)  |
| 77   | 268. | Seela and Kaiser, "Oligodeoxyribonucleotides containing 1,3-propanediol as nucleoside substitute," Nucleic Acids Research 15:3113-3129 (1987)   |
|      |      |   |

| EXAMINER DATE | TE CONSIDERED MILLS |
|---------------|---------------------|
|---------------|---------------------|

Sheet 25 of 29

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Com<br>Patent and Trademark | Atty. Docket No.   | Serial No. |
|------------------------------|--|--------------------|------------|
| , <b>(</b> ,                 |  | <br>02-742-F       | 10/665,951 |
|                              | INFORMATION DISCLOSURE                         | (400/132)          |            |
| 1                            | STATEMENT BY APPLICANT                         |                    |            |
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|                              |  | Applicant:         |            |
|                              |  | McSwiggen et al.   |            |
|                              |  | Filing Date:       | Group:     |
|                              |  | September 18, 2003 | 1635       |

| atts | 269. | Senger et al., "Vascular permeability factor (VPF, VEGF) in tumor biology," Cancer and Matastasis Reviews 12:303-324 (1993)  |
|------|------|--|
|      | 270. | Shabarova et al., "Chemical ligation of DNA: The first non-enyzmatic assembly of a biologically active gene," Nucleic Acids Research 19:4247-4251 (1991)   |
|      | 271. | Sharp, Philip A., "RNAi and Double-strand RNA", Genes and Development 13:139-141 (1999)  |
|      | 272. | Sheehan et al., "Biochemical properties of phosphonoacetate and thiophosphonoacetate oligodeoxyribonucleotides," <i>Nucleic Acids Research</i> , 31 (14), 4109-4118 (2003)   |
|      | 273. | Shifren et al., "Ovarian Steroid Regulation of Vascular Endothelial Growth Factor in the Human Endometrium: Implications for Angiogenesis during the Menstrual Cycle and in the Pathogenesis of Endometriosis," The Journal of Clinical Endocrinology & Metabolism 81:3112-3118 (1996) |
|      | 274. | Shweiki et al., "Patterns of Expression of Vascular Endothelial Growth Factor (VEGF) and VEGF Receptors in Mice Suggest a Role in Hormonally Regulated Angiogenesis," J. Clin. Invest. 91:2235-2243 (1993)   |
|      | 275. | Simantov et al., "Dopamine-Induced Apoptosis in Human Neuronal Cells: Inhibition by Nucleic Acids Antisense to the Dopamine Transporter," Neuroscience 74(1):39-50 (1996)  |
|      | 276. | Sommer et al., "The Spread and Uptake Pattern of Intracerebrally Administered Oligonucleotides in Nerve and Glial Cell Populations of the Rat Brain," Antisense & Nucleic Acid Drug Development 8:75-85 (1998)   |
|      | 277. | Strauss, Evelyn, "Molecular Biology: Candidate 'Gene Silencers' Found" Molecular Biology, 286: 5441, p.886 (1999)  |
|      | 278. | Sullenger and Cech, "Tethering Ribozymes to a Retroviral Packaging Signal for Destruction of Viral RNA," Science 262:1566-1569 (1993)  |
| 4    | 279. | Sun, "Technology evaluation: SELEX, Giliad Sciences Inc," Current Opinion in Molecular Therapeutics 2:100-105 (2000)   |

| EXAMINER Officer | DATE CONSIDERED | Dula |
|------------------|-----------------|------|
|                  |                 |      |

Sheet 26 of 29

| FORM PTO-1449<br>(Rev. 2-32) | Patent and Trademark Office | Atty. Docket No.<br>02-742-F<br>(400/132)                      | Serial No.<br>10/665,951 |
|------------------------------|-----------------------------|--|--------------------------|
|                              | (                           | Applicant:  McSwiggen et al.  Filing Date:  September 18, 2003 | Group:                   |

| arb      | 280. | Taira et al., "Construction of a novel RNA-transcript-trimming plasmid which can be used both in vitro in place of run-off and (G)-free transcriptions and in vivo as multi-sequences transcription vectors," Nucleic Acids Research 19:5125-5130 (1991) |
|----------|------|--|
|          | 281. | Takahashi et al., "Markedly Increased Amounts of Messenger RNAs for Vascular Endothelial Growth Factor and Placenta Growth Factor in Renal Cell Carcinoma Associated with Angiogenesis," Cancer Research 54:4233-4237 (1994)                             |
|          | 282. | Thomas et al., "Enhancing polyethylenimine's delivery of plasmid DNA into mammalian cells," PNAS, 99, 14640-14645 (2002)   |
|          | 283. | Thompson et al., "Improved accumulation and activity of ribozymes expressed from a tRNA-based RNA polymerase III promoter," Nucleic Acids Research 23:2259-2268 (1995)   |
|          | 284. | Turner et al., "Improved Parameters for Prediction of RNA Structure," Cold Spring Harbor Symposia on Quantitative Biology Volume LII, pp. 123-133 (1987)   |
|          | 285. | Turner et al., "Free Energy Increments for Hydrogen Bonds in Nucleic Acid Base Pairs," J. Am. Chem. Soc. 109:3783-3785 (1987)  |
|          | 286. | Tuschl et al., "Targeted mRNA Degradation by Double-Stranded RNA In Vitro," Genes & Development 13:3191-3197 (1999)  |
|          | 287. | Tuschl et al., "Small Interfering RNAs: A Revolutionary Tool for the Analysis of Gene Function and Gene Therapy," <i>Molecular Interventions</i> , 295, 3, 158-167 (2002)  |
|          | 288. | Tuschl, "RNA Interference and Small Interfering RNAs," Chembiochem 2:239-245 (2001)  |
|          | 289. | Tyler et al., "Peptide nucleic acids targeted to the neurotensin receptor and administered i.p. cross the blood-brain barrier and specifically reduce gene expression," Proc. Natl. Acad. Sci. USA 96:7053-7058 (1999)                                   |
| <u>/</u> | 290. | Tyler et al., "Specific gene blockade shows that peptide nucleic acids readily enter neuronal cells in vivo," FEBS Letters 421:280-284 (1998)  |

| EXAMINER | Otther   | DATE CONSIDERED WILLS |
|----------|--|-----------------------|
| L        | <del>- Y _ · · · U _ · · · · · · · · · · · · · ·</del> |                       |

| FORM PTO-1449<br>(Rev. 2-32)   | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.   | Serial No. |
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|                                |  | McSwiggen et al.   |            |
| ·                              |  | Filing Date:       | Group:     |
|                                |  | September 18, 2003 | 1635       |

|   | 295. | Usman et al., "Automated Chemical Synthesis of Long Oligoribonucleotides Using 2'-O-Silylated Ribonucleoside 3'-O-Phosphoramidites on a Controlled-Pore Glass Support: Synthesis of a 43-Nucleotide Sequence Similar to the 3'-Half Molecule of an Escherichia coli Formylmethoionine tRNA," J. Am. Chem. Soc. 109:7845-7854 (1987) |
|---|------|---|
|   | 296. | Am. Chem. Soc. 109:7845-7854 (1987)  Usman et al., "Chemical modification of hammerhead ribozymes: activity and nuclease resistance,"   |
|   |      | Nucleic Acids Syposium Series 31:163-164 (1994)   |
|   | 297. | Ventura et al., "Activation of HIV-Specific Ribozyme Activity by Self-Cleavage," Nucleic Acids Research 21:3249-3255 (1993)   |
|   | 298. | Verdel et al., "RNAi-Mediated Targeting ofHeterochromatin by the RITS Complex, Science, 303, 672-676 (2004)   |
|   | 299. | Verma and Eckstein, "Modified Oligonucleotides: Synthesis and Strategy for Users," Annu. Rev. Biochem. 67:99-134 (1998)   |
|   | 300. | Volpe et al., "Regulation of Heterochromatic Silencing and Histone H3 Lysine-9 Methylation by RNAi," Science 297:1833-1837 (2002)   |
|   | 301. | Waterhouse, et al. "Virus Resistance and gene Silencing in Plants Can Be Induced by Simultaneous Expression of Sense and Antisense RNA" Proc. Natl. Acad. Sci. USA 99:13959-13964 (1998)  |
| 1 | 302. | Weckbecker et al., "Intradermal angiogenesis in nude mice induced by human tumor cells or b-FGF," Angiogenesis Key Principles–Science–Technology–Medicine pp296-301 (1992)  |

| EXAMINER DAYS | DATE CONSIDERED |
|---------------|-----------------|
| (21) 10 0     | <u> </u>        |

**Sheet 28 of 29** 

| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce Patent and Trademark Office                         | Atty. Docket No.      | Serial No. |
|------------------------------|---|-----------------------|------------|
|                              | INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) | 02-742-F<br>(400/132) | 10/665,951 |
|                              | •   | Applicant:            |            |
|                              |   | McSwiggen et al.      |            |
| ·                            |   | Filing Date:          | Group:     |
|                              |   | September 18, 2003    | LATB HOST  |

| DAB | 303. | Weerasinghe et al., "Resistance to Human Immunodeficiency Virus Type 1 (HIV-1) Infection in Human CD4+ Lymphocyte-Derived Cell Lines Conferred by Using Retroviral Vectors Expressing an HIV-1 RNA-Specific Ribozyme," Journal of Virology 65:5531-5534 (1994) |
|-----|------|--|
|     | 304. | Wellstein and Czubayko, "Inhibition of Fibroblast Growth Factors," Breast Cancer Research and Treatment 38:109-119 (1996)`   |
| ·   | 305. | Wianny and Zernicka-Goetz et al., "Specific Interference with Gene Function by Double-Stranded RNA in Early Mouse Development," Nature Cell Biology 2:70-75 (2000)   |
|     | 306. | Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," Nucleic Acids Research 23(14):2677-2684 (1995)  |
|     | 307. | Wincott et al., "A Practical Method for the Production of RNA and Ribozymes," Methods in Molecular Biology 74:59-69 (1997)   |
|     | 308. | Woo et al., "Taxol Inhibits Progression of Congenital Polycystic Kindey Disease," Nature 368:750-753 (1994)  |
|     | 309. | Wu and Wu, "Receptor-mediated in Vitro Gene Transformation by a Soluble DNA Carrier System," The Journ. of Biol. Chem. 262:4429-4432 (1987)  |
|     | 310. | Wu et al., "Cardiac Defects and Renal Failure in Mice with Targeted Mutations in Pkd2," Nature Genetics 24:75-78 (2000)  |
|     | 311. | Wu-Pong et al., "Nucleic Acid Drug Delivery, Part 2; Delivery to the Brain," _ 32-38 (1999)  |
|     | 312. | Yamada et al., "Nanoparticles for the delivery of genes and drugs to human hepatocytes," Published online: 29 June 2003, doi:10.1038/nbt843 (August 2003 Volume 21 Number 8 pp 885-890) (2003)   |
|     | 313. | Yu et al., "A Hairpin Ribozyme Inhibits Expression of Diverse Strains of Human Immunodeficiency Virus Type 1," Proc. Natl. Acad. Sci. USA 90:6340-6344 (1993)  |
| . 7 | 314. | Zamore et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," Cell 101:25-33 (2000)  |
|     |      |  |

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| FORM PTO-1449<br>(Rev. 2-32) | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.   | Serial No. |
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|                              | STATEMENT BY APPLICANT                                     |                    |            |
|                              | (Use several sheets if necessary)                          |                    |            |
|                              |  | Applicant:         |            |
|                              |  | McSwiggen et al.   |            |
|                              |  | Fillng Date:       | Group:     |
|                              |  | September 18, 2003 | LHB 1635   |

| OHB    | 315. | Zhou et al., "Synthesis of Functional mRNA in Mammalian Cells by Bacteriophage T3 RNA Polymerase," Mol. Cell. Biol. 10:4529-4537 (1990)                  |
|--------|------|--|
| Cuthes | 316. | Ziche et al., "Angiogenesis Can Be Stimulated or Repressed In Vivo by a Change in GM3:GD3 Ganglioside Ratio," Laboratory Investigation 67:711-715 (1992) |

| EXAMINER | DATE CONSIDERED 10 11105 |
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